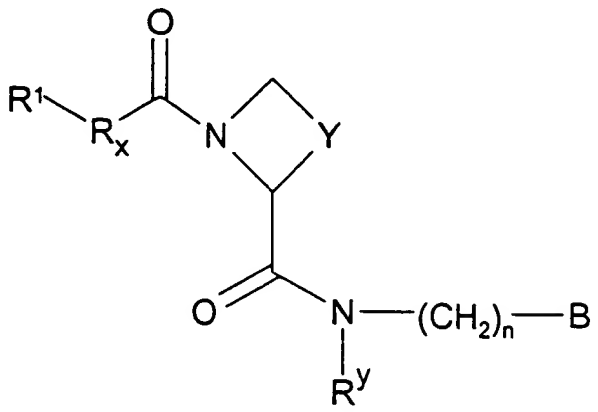
AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1 (currently amended). A compound of formula I,



I

wherein

R^1 represents H, C_{1-4} alkyl (optionally substituted by one or more substituents selected from cyano, halo, OH, $C(O)OR^{1a}$ or $C(O)N(R^{1b})R^{1c}$) or OR^{1d};

R^{1d} represents H, $C(O)R^{11}$, $SiR^{12}R^{13}R^{14}$ or C_{1-6} alkyl, which latter group is optionally substituted or terminated by one or more substituent selected from OR^{15} or $(CH_2)_qR^{16}$;

R^{12}, R^{13} and R^{14} independently represent H, phenyl or C_{1-6} alkyl;

R^{16} represents C_{1-4} alkyl, phenyl, OH, $C(O)OR^{17}$ or $C(O)N(H)R^{18}$;

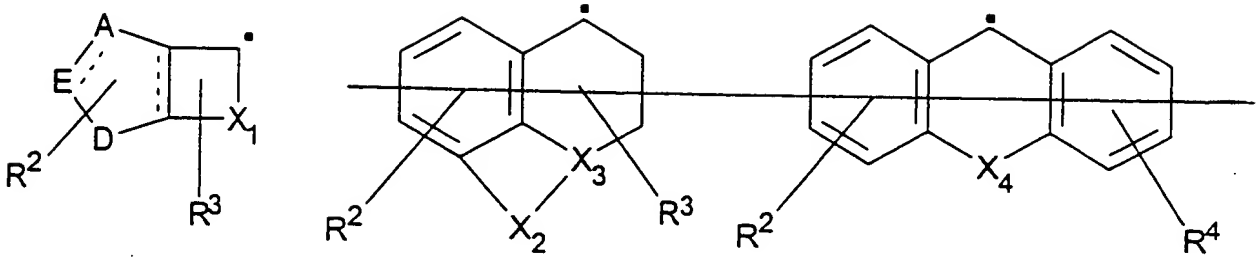
R^{18} represents H, C_{1-4} alkyl or $CH_2C(O)OR^{19}$;

R^{15} and R^{17} independently represent H, C_{1-6} alkyl or C_{1-3} alkylphenyl;

R^{1a}, R^{1b}, R^{1c}, R^{11} and R^{19} independently represent H or C_{1-4} alkyl; and

q represents 0, 1 or 2;

R_x represents a structural fragment of formula IIa, ~~IIb or IIc;~~



IIa IIb IIc

wherein

the dotted lines independently represent optional bonds;

A and E independently represent ~~O or S,~~ CH ~~or CH_2 (as appropriate), or N or $N(R^{21})$ (as appropriate)~~;

D represents ~~$-CH_2-$, O, S, $N(R^{22})$, $-(CH_2)_2-$,~~ -CH=CH-, ~~$-CH_2N(R^{22})-$, $-N(R^{22})CH_2-$, -CH=N-, -N=CH-, $-CH_2O-$, $-OCH_2-$, $-CH_2S-$ or $-SCH_2-$~~;

X_1 represents ~~C_{2-4} alkylene; C_{2-3} alkylene interrupted by Z; $-C(O)-Z-A^1-$; $-Z-C(O)-A^1-$; $-CH_2-C(O)-A^1-$; $-Z-C(O)-Z-A^2-$; $-CH_2-Z-C(O)-A^2-$; $-Z-CH_2-C(O)-A^2-$; $-Z-CH_2-S(O)_m-A^2-$; $-C(O)-A^3$; $-Z-A^3-$; or $-A^3-Z-$~~ $\underline{O-A^3}$;

~~X_2 represents C_{2-3} alkylene, $-C(O)-A^4-$ or $-A^4-C(O)-$;~~

~~X_3 represents CH or N;~~

~~X_4 represents a single bond, O, S, C(O), $N(R^{23})$, $-CH(R^{23})-$, $-CH(R^{23})-CH(R^{24})-$ or $-C(R)^{23})=C(R^{24})-$;~~

~~A^1 represents a single bond or C_{1-2} alkylene;~~

~~A^2 represents a single bond or $-CH_2-$;~~

A^3 represents C_{1-3} alkylene;

~~A^4 represents C(O) or C_{1-2} alkylene~~;

~~Z represents, at each occurrence, O, $S(O)_m$ or $N(R^{25})$~~;

R^2 ~~and R^4 independently represent~~ represents one or more optional substituents selected from C_{1-4} alkyl, C_{1-4} alkoxy (which latter two groups are optionally substituted by one or more halo substituent), methylenedioxy, halo, hydroxy, cyano, nitro, $S(O)_2NH_2$, $C(O)OR^{26}$, SR^{26}, $S(O)R^{26a}$, $S(O)_2R^{26a}$ or $N(R^{27})R^{28}$;

R^3 represents one or more optional substituents selected from OH, C_{1-4} alkoxy, C_{1-6} alkyl (optionally substituted by one or more halo group), or $N(R^{29a})R^{29b}$;

~~R^{25}~~, R^{29a} and R^{29b} independently represent H, C_{1-4} alkyl or $C(O)R^{30}$;

R^{26} represents H or C_{1-4} alkyl;

R^{26a} represents C_{1-4} alkyl;

R^{27} and R^{28} independently represent H, C_{1-4} alkyl or $C(O)R^{30}$, or together represent C_{3-6} alkylene, thus forming a 4- to 7-membered ring, which ring is optionally substituted, on a carbon atom that is α to the nitrogen atom, with an =O group;

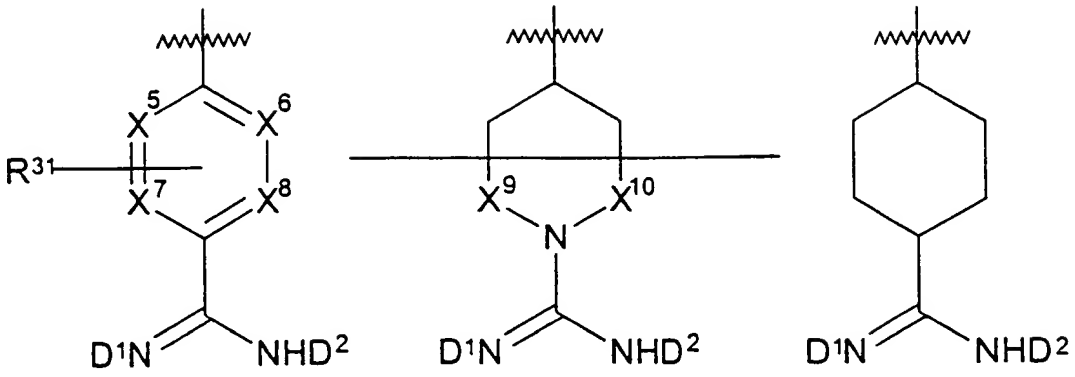
~~R^{21}, R^{22}, R^{23}, R^{24} and~~ R^{30} ~~independently represent~~ represents, at each occurrence, H or C_{1-4} alkyl;

Y independently represents CH_2, $(CH_2)_2$, or CH=CH ~~(which latter group is optionally substituted by C_{1-4} alkyl), $(CH_2)_3$, $CH_2CH=CH$ or $CH=CHCH_2$ (which latter three groups are optionally substituted by C_{1-4} alkyl, methylene, =O or hydroxy)~~;

R^y represents H or C_{1-4} alkyl;

n represents 0, 1, 2, 3 or 4; and

B represents a structural fragment of formula IIIa~~, IIIb~~ or IIIc



IIIa IIIb IIIc

wherein

X^5, X^6, X^7 and X^8 independently represent CH~~, N or N-O~~;

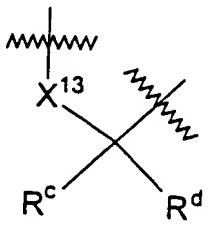
~~X^9 and X^{10} independently represent a single bond or CH_2;~~

R^{31} represents an optional substituent selected from halo, C_{1-4} alkyl (which group is optionally substituted by one or more halo group), $N(R^{32})R^{33}$, OR^{34} or SR^{35};

R^{32} and R^{33} independently represent H, C_{1-4} alkyl or $C(O)R^{36}$;

R^{34}, R^{35} and R^{36} independently represent H or C_{1-4} alkyl; and

one of D^1 and D^2 represents H, and the other represents H, OR^a, NHR^a, $C(=X^{11})X^{12}R^b$, or D^1 and D^2 together represent a structural fragment of formula IVa:-



IVa

R^a represents H or $-A^5[X^{14}]_n[C(O)]_rR^e$;

R^b represents $-A^5[X^{14}]_n[C(O)]_rR^e$;

A^5 represents, at each occurrence, a single bond or C_{1-12} alkylene (which alkylene group is optionally interrupted by one or more O, $S(O)_m$ and/or $N(R^f)$ group, and is optionally substituted by one or more of halo, OH, $N(H)C(O)R^g$, $C(O)N(R^g)R^h$, C_{3-7}-cycloalkyl (which cycloalkyl group is optionally interrupted by one or more O, $S(O)_m$ and/or $N(R^f)$ group and/or is optionally substituted by one or more substituents selected from C_{1-6} alkyl, C_{1-6} alkoxy, halo, =O or =S), Het and C_{6-10} aryl (which aryl and Het groups are themselves optionally substituted by one or more substituents selected from C_{1-6} alkyl (optionally substituted by one or more halo substituent), C_{1-6} alkoxy, halo, cyano, $C(O)OR^g$, $C(O)N(R^g)R^h$ and $N(R^f)R^g$));

R^c and R^d both represent H; or one of R^c and R^d represents H or C_{1-7} alkoxy and the other represents C_{1-7} alkyl (which alkyl group is optionally interrupted by one or more O atoms); or R^c and R^d together represent C_{3-8} cycloalkyl, which cycloalkyl group is interrupted by one or more O, $S(O)_m$ and/or $N(R^f)$ group;

R^e represents, at each occurrence, H, C_{1-12} alkyl (which alkyl group is optionally interrupted by one or more O, $S(O)_m$ and/or $N(R^f)$ group, and/or is optionally substituted by one or more substituents selected from halo, OH, $N(H)C(O)R^g$ and $C(O)N(R^g)R^h$), A^7-C_{3-7}-cycloalkyl (which cycloalkyl group is optionally interrupted by one or more O, $S(O)_m$ and/or $N(R^f)$ group and/or is substituted by one or more substituents selected from C_{1-6} alkyl, C_{1-6} alkoxy, halo, =O and =S), A^7-C_{6-10} aryl or A^7-Het (which aryl and Het groups are optionally substituted by one or more substituents selected from C_{1-6} alkyl (optionally substituted by one or more halo substituent), C_{1-6} alkoxy, halo, cyano,

$C(O)OR^g$, $C(O)N(R^g)R^h$ and $N(R^f)R^g$);

A^7 represents a single bond or C_{1-7} alkylene (which alkylene group is optionally interrupted by one or more O, $S(O)_m$ and/or $N(R^f)$ group, and/or are optionally substituted by one or more of halo, OH, $N(H)COR^g$ and $CON(R^g)R^h$);

Het represents, at each occurrence, a five- to ten-membered heteroaryl group, which may be aromatic in character, containing one or more nitrogen, oxygen or sulphur atoms in the ring system;

n and r independently represent 0 or 1;

X^{11}, X^{12} and X^{14} independently represent O or S;

X^{13} represents O or $N(R^f)$;

R^f represents, at each occurrence, H, C_{1-4} alkyl or $C(O)R^g$;

R^g and R^h independently represent, at each occurrence, H or C_{1-4} alkyl; and

m represents, at each occurrence, 0, 1 or 2;

or a pharmaceutically acceptable salt thereof;

provided that:

~~(a) A and E do not both represent O or S;~~

~~(b) E and D do not both represent O or S;~~

~~(c) when R^1 represents OR^{1d} and X_1 represents $-C(O)-Z-A^1-$, $-Z-CH_2-S(O)_m-A^2-$ or $-Z-C(O)-Z-A^2-$, then A^1 or A^2 (as appropriate) do not represent a single bond;~~

~~(f) when X_4 represents $-CH(R^{23})-$, R^1 does not represent OH;~~

~~(g)~~ when A^5 represents a single bond, then n and r both represent 0;

~~(t)~~ when A^5 represents C_{12} alkylene, then n represents 1;

~~(g)~~ when A^5 represents $-CH_2-$, n is 1 and r is 0, then R^e does not represent H; and

~~(h)~~ the compound is not:-

(S)- or *(R)*-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Pro-Pab;

(R)- or *(S)*-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Pro-Pab;

(S)- or (R)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab x HOAc;

(R)- or *(S)*-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab;

1-hydroxy-5-methoxytetralin-1-yl-C(O)-Aze-Pab x HOAc;

1-hydroxy-5,7-dimethyltetralin-1-yl-C(O)-Aze-Pab x HOAc;

1-hydroxy-7-aminotetralin-1-yl-C(O)-Aze-Pab x HOAc;

1-hydroxytetralin-1-yl-C(O)-Aze-Pab x HOAc;

7-methoxytetralin-1-yl-C(O)-Aze-Pab x HOAc;

(R)- or *(S)*-7-methoxy-1-methyltetralin-1-yl-C(O)-Aze-Pab;

4-hydroxy-6-methoxychroman-4-yl-C(O)-Aze-Pab x OAc;

(S)- or *(R)*-1-hydroxy-4-methoxyindan-1-yl-C(O)-Aze-Pab;

1-hydroxy-5-methoxytetralin-1-yl-C(O)-Aze-Pab(OH);

(S)- or *(R)*-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(OH);

4-hydroxy-6-methoxychroman-4-yl-C(O)-Aze-Pab(OH);

4-hydroxy-6-methoxychroman-4-yl-C(O)-Aze-Pab(OMe);

(S)- or *(R)*-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab-$(C(O)OCH_2CC1_3)$;

(S)- or *(R)*-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab-$(C(O)OCH_2CH_3)$;

7-methoxy-1-allyltetralin-1-yl-C(O)-Aze-Pab x HOAc;

(S)- or *(R)*-1-hydroxy-7-chlorotetralin-1-yl-C(O)-Pro-Pab;

1-*n*-propyl-7-methoxytetralin-1-yl-C(O)-Aze-Pab x HOAc;

6-chloro-4-hydroxychroman-4-yl-C(O)-Aze-Pab x HOAc;

4-hydroxychroman-4-yl-C(O)-Aze-Pab x HOAc;

6 ,8-dichloro-4-hydroxychroman-4-yl-C(O)-Aze-Pab x HOAc;

6-fluoro-4-hydroxychroman-4-yl-C(O)-Aze-Pab x HOAc;

4-hydroxy-6-methylchroman-4-yl-C(O)-Aze-Pab x HOAc;

8-chloro-4-hydroxy-6-methoxychroman-4-yl-C(O)-Aze-Pab x HOAc;

6-chloro-4-hydroxy-8-methylcbroman-4-yl-C(O)-Aze-Pab x HOAc;

(S)- or *(R)*-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(O-C(O)-*i*-Pr);

(S)- or *(R)*-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(O-C(O)-Et);

(S)- or *(R)*-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(O-C(O)-Ch);

(S)- or *(R)*-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(O-allyl);

(S)- or *(R)*-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(O-Bzl);

(S)- or *(R)*-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab-
(CO-O-methallyl);

1-hydroxy-7-aminotetralin-1-yl-C(O)-Aze-Pab(OH);

(S)- or *(R)*-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(O-Val);

(S)- or *(R)*-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-(Me)Pab; or

9-hydroxyfluoren-9-yl-C(O)-Aze-Pab x HOAc.

2 (previously presented). A compound as claimed in Claim 1 wherein R^1

represents OH or C_{1-4} alkyl (which latter group is optionally substituted by cyano or OH).

3 (cancelled).

4 (currently amended). A compound as claimed in claim 1 wherein~~, when R_x represents a structural fragment of formula IIa, then~~ the dotted lines represent bonds~~, A and E both represent CH and D represents -CH=CH-~~;.

5 (currently amended). A compound as claimed in claim 1 wherein~~,~~ ~~when R_x represents a structural fragment of formula IIa, X_1 optionally unsaturated C_2- or C_3-alkylene, or -Z-A^3 (in which Z represents O, $S(O)_m$ or $N(R^{25})$ (in which R^{25} is as defined in Claim 1 or represents C_{1-4} alkyl or $C(O)R^{30}$ and m and R^{30} are as defined in Claim 1) and~~ A^3 represents C_1- or C_2-alkylene ~~(which latter group is optionally unsaturated))~~.

6 (currently amended). A compound as claimed in claim 1 wherein Y represents CH_2~~,~~ or $(CH_2)_2$ ~~or $(CH_2)_3$~~.

7 (previously presented). A compound as claimed in claim 1 wherein B represents a structural fragment of formula IIIa in which X^5, X^6, X^7 and X^8 all represent CH.

8 (previously presented). A compound as claimed in claim 1 wherein, when D^1

and D^2 together represent a structural fragment of formula IVa, in which X^{13} is O, then one of R^c and R^d represents H or C_{17} alkoxy and the other represents C_{1-7} alkyl.

9 (previously presented). A compound as claimed in claim 1, wherein, when D^1 or D^2 represents OR^a and R^a represents $-A^5[X^{14}]_n[C(O)]_r R^e$, and

(i) A^5 is a single bond, then R^e is:-

(1) A^7-aryl, optionally substituted by one or more halo, C_{1-6} alkoxy, C_{1-6} alkyl or halo-C_{1-6}-alkyl substituents; or

(2) H or linear, branched, optionally unsaturated, and/or cyclic, C_{1-2} alkyl, which cyclic alkyl group is optionally interrupted by an O atom and, optionally, a further O atom or $S(O)_m$ group; or when

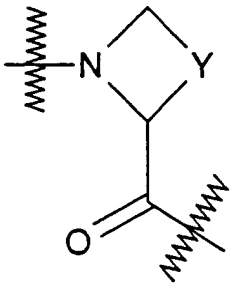
(ii) A^5 is linear or branched C_{1-12} alkylene, X^{14} is O and r is 0, then R^e is C_{1-3} alkyl or A^7-aryl, in which A^7 is a single bond.

10 (previously presented). A compound as claimed in claim 1, wherein, when D^1 or D^2 represents OR^a, then R^a is H or C_{1-4} alkyl.

11 (previously presented). A compound as claimed in claim 1, wherein, when D^1 or D^2 represents $-C(=X^{11})X^{12}R^b$, in which X^{11} represents O and X^{12} represents O or S, and, in which R^b group, A^5 represents a single bond then R^e represents optionally unsaturated C_{1-6} alkyl, A^7-C_{6-10}-aryl (in which A^7 represents a single bond or C_{1-2} alkylene, and which A^7-C_{6-10}-aryl group is optionally substituted by one or more halo, C_{1-4} alkyl and/or C_{1-4} alkoxy groups), or A^7-C_{3-7}-cycloalkyl, in which A^7 represents a

single bond or linear or branched C_{1-7} alkylene, and which cycloalkyl group is optionally substituted by C_{1-3} alkyl.

12 (previously presented). A compound of formula I, as defined in claim 1, wherein the fragment



is in the S-configuration.

13 (previously presented). A pharmaceutical formulation including a compound as defined in claim 1, or a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

14-20 (cancelled).

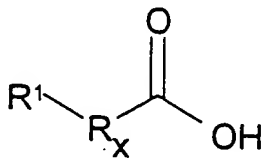
21 (previously presented). A method of treatment of a condition where inhibition of thrombin is required which method comprises administration of a therapeutically effective amount of a compound as defined in claim 1, or a pharmaceutically acceptable salt thereof, to a person suffering from, or susceptible to, such a condition.

22 (previously presented). A method as claimed in Claim 21, wherein the condition is thrombosis.

23 (previously presented). A method as claimed in Claim 21, wherein the condition is hypercoagulability in blood and tissues.

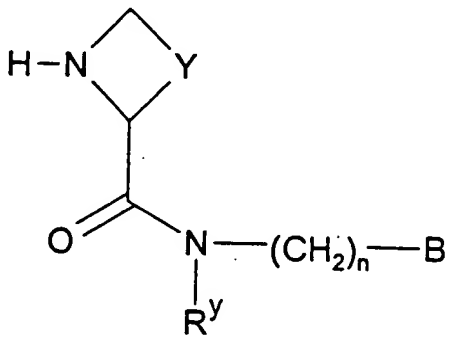
24 (currently amended). A process for the preparation of compounds of formula I which comprises:

(i) the coupling of a compound of formula IV,



IV

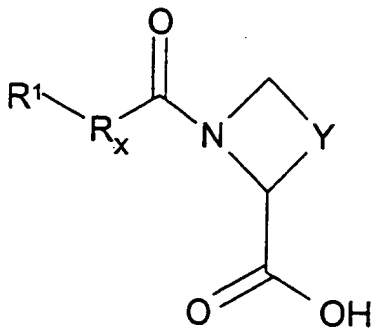
wherein R^1 and R_x are as defined in Claim 1 with a compound of formula V,



V

wherein R^y, Y, n and B are as defined in Claim 1;

(ii) the coupling of a compound of formula VI,



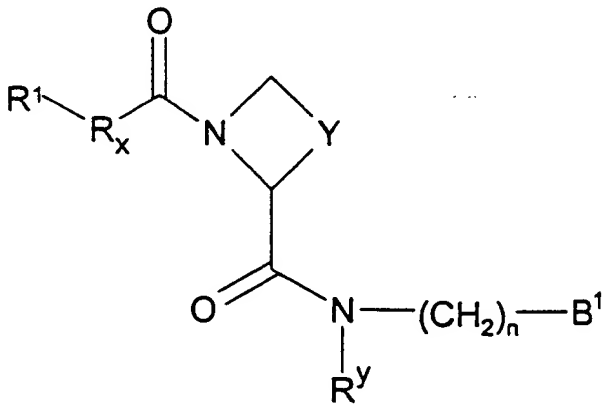
VI

wherein R^1, R_x and Y are as defined in Claim 1 with a compound of formula VII,

$$H(R^y)N\text{-}(CH_2)_n\text{-}B \qquad \text{VII}$$

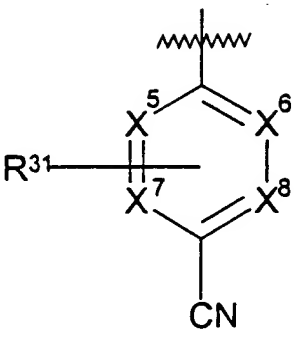
wherein R^y, n and B are as defined in Claim 1;

(iii) for compounds of formula I in which D^1 or D^2 represents OR^a or NHR^a, reaction of a compound of formula VIII,



VIII

wherein B^1 represents a structural fragment of formula IIId, ~~IIIe~~ or IIIf



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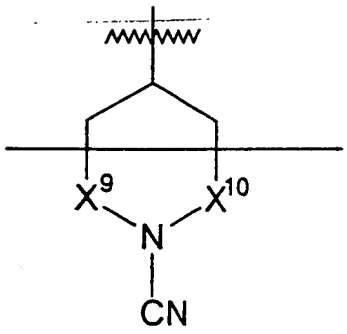
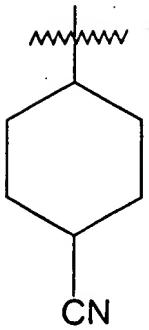


IIIe



IIIf

and R^1, R_x, Y, R^y, n, R^{31}, X^5, X^6, X^7, and X^8, ~~X^9 and X^{10}~~ are as defined in Claim 1 with a compound of formula IX,

$$H_2NX^aR^a \qquad IX$$

wherein X^a represents O or NH and R^a is as defined in Claim 1;

(iv) for compounds of formula I in which D^1 or D^2 represents OR^a or NHR^a, reaction of a compound of formula I in which D^1 or D^2 (as appropriate) represents $C(O)OR^{b1}$, in which R^{b1} represents a protecting group with a compound of formula IX as defined above;

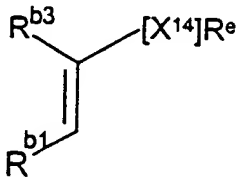
(v) for compounds of formula I in which D^1 or D^2 represents OR^a or NHR^a, R^a represents $-A^5[X^{14}]_n[C(O)]_rR^e$, in which A^5 does not represent a single bond, and n represent 1, reaction of a compound of formula I in which D^1 or D^2 (as appropriate) represents OH or NH_2, with a compound of formula X,

$$L^1A^{5a}[X^{14}][C(O)]_rR^e \qquad X$$

wherein L^1 represents a suitable leaving group, A^{5a} represents A^5, as defined in Claim 1 except that it does not represent a single bond, and X^{14}, r and R^e are as defined

in Claim 1;

(vi) for compounds of formula I in which D^1 or D^2 represents OR^a or NHR^a, R^a represents $-A^5[X^{14}]_n[C(O)]_rR^e$, in which A^5 represents C_{2-12} alkylene, which alkylene group is branched at the carbon atom that is α to the O or N atom of OR^a or NHR^a (as appropriate), and which group is optionally branched at the carbon atom that is β to that atom, n represents 1, r represents 0 and R^e is as defined in Claim 1, reaction of a compound of formula I in which D^1 or D^2 (as appropriate) represents OH or NH_2, with a compound of formula XI,

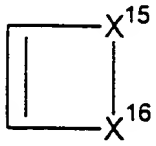


XII

or a geometrical isomer thereof, or a mixture of such geometrical isomers, in which R^{b1} and R^{b3} each represent H or an alkyl group, provided that the total number of carbon atoms provided by R^{b1} and R^{b3} does not exceed 10, and wherein X^{14} and R^e are as defined in Claim 1;

(vii) for compounds of formula I in which D^1 or D^2 represents OR^a or NHR^a, R^a represents $-A^5[X^{14}]_n[C(O)]_rR^e$, in which A^5 represents a single bond, and R^e represents A^7-C_{3-6}-cycloalkyl, in which A^7 represents a single bond, and the cycloalkyl group is interrupted by at least one O or S atom, which atom is between the carbon atom at the point of attachment to the O or NH group of OR^a or NHR^a, and a carbon atom that is α

to that point of attachment, and which cycloalkyl group is optionally interrupted by one or more O or $S(O)_m$ group and/or optionally substituted by one or more =O group, reaction of a compound of formula I, in which D^1 or D^2 (as appropriate) represents OH or NH_2, with a compound of formula XII,



XII

wherein X^{15} represents O or S and X^{16} represents C_{1-4} alkylene (which alkylene group is optionally interrupted by one or more O or $S(O)_m$ group and/or optionally substituted by one or more =O group);

(viii) for compounds of formula I in which D^1 or D^2 represents $C(X^{11})X^{12}R^b$, reaction of a compound of formula I in which D^1 and D^2 both represent H with a compound of formula XIII,

$$L^2\text{-}C(X^{11})X^{12}R^b \qquad \text{XIII}$$

wherein L^2 represents a suitable leaving group, and X^{11}, X^{12} and R^b are as defined in Claim 1;

(ix) for compounds of formula I in which D^1 and D^2 together represent a structural fragment of formula IVa, reaction of a corresponding compound of formula I in which D^1 or D^2 represents OH or NHR^f (in which R^f is as defined in Claim 1), with a compound of formula XV,

$$(R^c)(R^d)C(R^{c1})(R^{c2}) \qquad \text{XV}$$

wherein R^{c1} and R^{c2} both represent $-OR^{c3}$, in which R^{c3} represents C_{1-3} alkyl, or together represent =O, and R^c and R^d are as defined in Claim 1;

(x) for compounds of formula I in which one or more of X^5, X^6, X^7 and X^8 represent N-O, oxidation of a corresponding compound of formula I in which X^5, X^6, X^7 and/or X^8 (as appropriate) represent(s) N; or

(xi) for compounds of formula I in which any one of Z, X_1, R^2, R^4, A^5, A^7, R^C, R^d and/or R^e comprises or includes a S(O) or a $S(O)_2$ group, oxidation of a corresponding compound of formula I (or a compound corresponding to a compound of formula I) wherein Z, X_1, R^2, R^4, A^5, A^7, R^c, R^d and/or R^e (as appropriate) comprise(s) or include(s) a S group;

(xii) for compounds of formula I in which D^1 and D^2 both represent H, removal of a OR^a, NHR^a or $C(=X^{11})X^{12}R^b$ group (in which R^a, R^b, X^{11} and X^{12} are as defined in Claim 1), or removal of a structural fragment of formula IVa as defined in Claim 1, from a corresponding compound of formula I; or

(xiii) introduction and/or interconversion of a substituent on an aromatic and/or non-aromatic, carbocyclic and/or heterocyclic ring in a corresponding compound of formula I.